65. (Amended) [The method of] A host cell for producing an infectious attenuated chimeric RSV comprising a mammalian cell susceptible to RSV infection transfected or transformed with an expression vector according to claim 64[, wherein the chimeric RSV genome or antigenome and the N, P, L and RNA polymerase elongation factor proteins are expressed by two or more different expression vectors].

REMARKS

With Entry of this Amendment, claims 1-35, and 46-65 are pending in the application. By this Amendment, claims 1-3, 52-54, 64, and 65 have been amended and claims 36-45 canceled (withdrawn from consideration), without prejudice.

Subject matter presented within the claims as amended is believed to correspond generically to group I set forth in the Restriction Requirement, which is hereby elected with traverse by way of presentation of the amended claims herein.

The present Amendment is intended to resolve restriction practice issues in this application following the course of informal telephone interviews conducted with Examiner Brumback on October 2, 2000 and November 7, 2000. The focus of these interviews was to request clarification and reconsideration of the Restriction Requirement by the Examiner, to determine an efficient, consistent process for examining the subject matter of the application in a manner that does not present an undue burden on either the Office or Applicants.

It was noted during these interviews that two Restriction Requirements, pending in this case and in a related (Serial No. 09/444,067) ('067) application based on a common parent application Serial No. 08/892,403 ('403) (now issued as U.S. Patent No. 5,993,824 ('824)), proscribe a total of 33 separate groups initially proposed to constitute separate and distinct inventions. It was further noted that a Restriction Requirement in the parent, '403 application set forth only 9 groups proposed as distinct inventions. One of these groups (recombinant RSV incorporating temperature sensitive mutations) was elected and prosecuted to become the issued '824 patent. Another group specified in the parental Restriction Requirement, group II (relating to gene deletion/ablation mutants) was generally elected as the

foundational subject matter of claims in the '067 application. Yet another application is on file with the Office (Serial No. 09/444,221) presenting claims directed to additional subject matter restricted in the parent case (RSV with modification to a cis-acting regulatory sequence such as a promoter, GS or GE signal sequence). All three of these applications are commonly assigned to Examiner Brumback for review.

Applicants requested during the above-noted interviews that the proposed restrictions in the present application, as well as in the related applications pending before Examiner Brumback, be reconsidered in an effort to avert the high costs, inefficiency, and potentially inconsistent examination that might attend separate prosecution of the various restricted groups. In this regard, Applicants' representative submitted that many of the restricted groups relate to species that can be examined together. In particular, it was suggested that certain dependent and "combinatorial" aspects of the invention are sufficiently related that they would not create an undue burden on the Office to examine them coordinately. Notably, many of these dependent and combinatorial aspects within the generic invention are independently claimed in related applications which are, or may prospectively be, assigned to Examiner Brumback—hopefully minimizing any additional searching and examination burdens that might otherwise attend their coordinate prosecution.

During the course of the above-referenced interviews, Examiner Brumback made numerous helpful suggestions which clarified the course of restriction practice in the application. The present Amendment is now filed in reply to these suggestions, hoping to follow faithfully the proposals made by the Examiner to advance the case to substantive prosecution.

As an initial point, Examiner Brumback courteously specified during the November 7, 2000 interview that it would not be fruitful to maintain co-prosecution of claims directed to human-human and human-non-human (e.g., human-bovine) RSV chimeras. In response, Applicants have amended the claims herein for clarity to focus on human-human RSV chimeras, withdrawing from consideration, without prejudice, the non-elected subject

matter exemplified by human-bovine chimeric RSV recombinant vaccines. Applicants reserve the right to file a divisional or other related application to this non-elected subject matter.

Examiner Brumback also indicated during the interview that it would not be fruitful to maintain co-prosecution of claims directed to recombinant RSV compositions alongside claims to methods for producing recombinant RSVs, and methods for stimulating an immune response involving administration of the recombinant viruses. In response, Applicants have canceled or amended the claims herein for clarity to withdraw, without prejudice, claims directed to methods for stimulating an immune response (claims 36-45) and to methods for producing recombinant RSVs (claims 64 and 65). Applicants reserve the right to file one or more divisional or other related application(s) to this non-elected subject matter.

Examiner Brumback also kindly indicated that it would not impose and undue burden on the Office to examine together certain closely related subject matter, as exemplified by the following groups: recombinant, chimeric viruses; isolated polynucleotides encoding the recombinant, chimeric viral genome; vectors incorporating these polynucleotides; and host cells transfected or transformed by the foregoing vectors. Thus, claims have been maintained or added herein to embrace these related aspects of the invention for coordinate prosecution. Following this direction by the Examiner, Applicants' representative submitted during the November 7, 2000 interview that claims to immunogenic compositions containing the foregoing recombinant viruses might also be prosecuted coordinately with the foregoing groups without undue burden. It is noted in this context that the issued '824 patent from the '403 parent application includes claims that span a similar range of related subject matter

With regard to claims which present dependent or "combinatorial" aspects of the invention, the Examiner stated a general agreement that these aspects of the invention could be viewed as "species" within a defined genus. For example, a genus defined as human A/B chimeric RSV may incorporate one or more different heterologous gene(s) or genome segment(s) (e.g., of NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F or G) within the background genome or antigenome. Such exemplary constructs disclosed in the application include single or multiple gene substitutions involving the RSV F and/or G glycoproteins to

generate a chimeric (mono- or poly-specific) RSV A/B vaccine candidate. In more detailed aspects, a particular genome segment (e.g., a glycoprotein ectodomain) may be exchanged or introduced to form the chimeric genome. These dependent aspects are believed sufficiently related that their common examination would not impose an undue burden on the Office. In particular, searching and review of published materials relating to human-human chimeric RSV is expected to largely comprehend the art relating to species of human-human chimeric RSV, for example have additional modifications, as presently claimed. This is particularly true if separate applications directed independently to these aspects, only claimed in the present application as dependent, "combinatorial" aspects within a defined genus, are before the Examiner simultaneously.

The important "combinatorial" aspects of Applicants' invention cannot be efficiently dissected away from Applicant's generic invention defined, e.g., by a recombinant human RSV A/B chimera. In this regard, Applicants' invention depends in specific embodiments on the use of a combination of modifications selected from a diverse "menu" of useful genetic manipulations—to provide an optimal, live-attenuated vaccine candidate for a selected population of target vacinees (e.g., seronegative versus seropositive infants). In this context, it will often be desired, for example, to combine the basic RSV A/B chimeric construction with one or more attenuating mutations, or other nucleotide changes, that specify a desired phenotype. In this regard, Applicants have clearly shown how to introduce temperature-sensitive and other types of attenuating point mutations (see, e.g., groups IV-VI), as well as gene deletions (e.g., group VII) and other changes (e.g., group VIII), into chimeric human RSV. These and other combinatorial-designed viruses are fully supported by the disclosure and Examples of the specification.

For the foregoing reasons, Applicants respectfully submit that the claims presented herein are consistent with the provisions and policies governing restriction practice in the PTO, particularly with regard to coordinate presentation and examination of genus/species claims. Collective examination of these claims is therefore earnestly solicited.

The Examiner is kindly invited to telephone the undersigned at 206-467-9600 if further discussion of the foregoing restriction practice issues is desired.

Respectfully submitted,

Date: 11/7/00 By: _____

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